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# Reduction of Carbon-Carbon Double Bonds using Organocatalytically Generated Diimide

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**General:**  $^1\text{H}$ -NMR spectra were recorded at 300 or 400 MHz with  $\text{CDCl}_3$  as solvent. Progress and conversion of the reactions was determined by GC-MS equipped with an HP1 column.

**Materials:** Riboflavin, acetaldehyde, palladium (10%) on activated carbon,  $\text{H}_2\text{NNH}_2 \cdot \text{H}_2\text{O}$ , methyl-*p*-tolylsulfide, 1-decene, 1,6-heptadien-4-ol, norbornylene, cis-cyclooctene, 1-(1-ethynyl)-1-cyclohexene, styrene, 4-allyl-2-methoxyphenol (eugenol), 2-vinylpyridine, allyl phenyl sulfide, trans-stilbene, 3,7-dimethyl-6-octadien-3-ol (linalool), geraniol, (+)- and (-)-limonene, 10-undecen-1-ol and chlorotrityl chloride polymer resin were commercially available and used without further purification. (-)-(((S)-2-methylbut-3-enyloxy)methyl)benzene (**18a**) was generously donated by A.W. van Zijl,<sup>1</sup> benzyl diallylcarbamate was prepared according to a literature procedure.<sup>2</sup>

The products decane, propyl phenyl sulfide and dihydrolinalool have been previously described (see appropriate references in the following pages) following a similar reaction procedure. The hydrogenation of the olefins was followed by GC-MS, conversion was calculated based on disappearance of the signal of the substrate and appearance of a signal corresponding to the product(s). Both the GC-MS library and observed mass were used to confirm the identity of the products. The volatile products 4-heptanol, norbornane, and cyclooctene were not isolated. The products 1-ethyl cyclohexene, 2-methoxy-4-propylphenol, 2-ethylpyridine, citronellol, 3,7-dimethyl-1-hydroxy-2-octene, 3,7-dimethyl-1-octanol, *N*-(benzyloxycarbonyl)dipropylamine, (+) and (-)-1-ethyl-4-isopropylcyclohexene and 1-undecanol afforded  $^1\text{H}$  NMR spectra identical to literature.

**Note:** GC-MS analysis was carried out on samples passed through a short plug of  $\text{MgSO}_4$  to remove hydrazine, diimide and water.

**Typical Procedure for the hydrogenation of an olefin with 20 equiv of hydrazine monohydrate and 5 mol% of flavin catalyst 1a.**

A mixture of olefin (0.5 mmol), flavin catalyst **1a** (10.0 mg, 0.025 mmol), and  $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$  (0.5 g, 11 mmol) in ethanol (4.0 mL) was stirred vigorously at 25 °C under air. Samples of 200  $\mu\text{L}$  were eluted with ethanol over a short  $\text{MgSO}_4$  column and subjected to GC-MS analysis.

**4-heptanol (5b):** conversion and purity (>95%) based on GC-MS analysis after 4 h. No side products were observed.

**cyclooctane (3b):** conversion and purity (>95%) based on GC-MS analysis after 4 h. No side products were observed.

**1-ethylcyclohexene(7b)<sup>3</sup>:** conversion and purity (>95%) based on GC-MS analysis after 4 h. No side products were observed.

**Ethylbenzene (8b)<sup>4</sup>:** conversion and purity (>95%) based on GC-MS analysis after 4 h. No side products were observed.

**n-Butylbenzene (9b)<sup>5</sup>:** Purification by extraction with 4x 5 ml pentane followed by washing of the organic layer with brine and evaporation of the solvent afforded a yellow oil. (99% yield)  $^1\text{H-NMR}$   $\delta$  7.05-7.35 (m, 5H), 5.5 (t, 2H), 1.05-1.80 (m, 4H), 0.9 (t, 3H). >95% (GC-MS).

**2-methoxy-4-propylphenol (10b)<sup>6</sup>:** Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. [78% yield]  $^1\text{H-NMR}$   $\delta$  6.83 (m, 1H), 6.67 (m, 2H), 5.52 (s, 1H), 3.86 (s, 3H), 2.57 (t,  $J$  = 7.61 Hz, 2H), 1.61 (m, 2H), 0.92 (m, 3H);  $^{13}\text{C-NMR}$   $\delta$  146.5 (C), 143.8 (C), 134.9 (C), 121.2 (CH), 114.3 (CH), 111.3 (C), 56.1 ( $\text{CH}_3$ ), 38.0 ( $\text{CH}_2$ ), 25.1 ( $\text{CH}_2$ ), 14.0 ( $\text{CH}_3$ ). >95% (GC-MS). HRMS calcd for  $\text{C}_{10}\text{H}_{15}\text{O}_2$  167.1066, found 167.1069

**2-ethylpyridine(11b)<sup>7</sup>:** Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. [73% yield]  $^1\text{H-NMR}$   $\delta$  8.52 (d,  $J$  = 4.8 Hz, 1H), 7.59 (m, 1H), 7.16 (d,  $J$  = 4.8 Hz, 1H), 7.09 (m, 1H), 2.83 (q,  $J$  = 7.6 Hz, 2H), 1.31 (m, 3H);  $^{13}\text{C-NMR}$   $\delta$  165.3 (C), 149.4 (CH), 136.6 (CH), 122.2 (CH), 121.1 (CH), 31.6 ( $\text{CH}_2$ ), 14.1 ( $\text{CH}_3$ ). >95% (GC-MS). HRMS calcd for  $\text{C}_7\text{H}_{10}\text{N}$  108.0807, found 108.0817

**propyl phenyl sulfide(12b):** Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil (99 % yield, >95% (GC-MS)).

**Citronellol (15b)<sup>8a</sup> /3,7-dimethyl-1-hydroxy-2-octene (15c):** Conversion based on GC-MS data. Except for the expected 3,7-dimethyl-1-hydroxy-2-octene, no other products were observed.

**3,7-dimethyl-1-octanol (15d)<sup>8b</sup>:** Conversion based on GC-MS data. Except for the expected 3,7-dimethyl-1-octanol, no other products were observed.

**Benzenepropanoic acid,  $\beta$ -methyl-, ethyl ester (16b)<sup>9</sup>:** Conversion based on GC-MS data.

**N-(Benzyloxycarbonyl)dipropylamine (17b)<sup>10</sup>:** Purification by extraction with 4x 5 ml ethyl acetate followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. (90% yield)  $^1\text{H-NMR}$   $\delta$  7.30 (m, 5H), 5.11 (s, 2H), 3.18 (br s, 4H), 1.54 (br s, 4H), 0.85 (br, 6H);  $^{13}\text{C-NMR}$   $\delta$  137.6 (C), 128.9 (CH), 128.2 (CH), 128.1 (CH), 110.3 (CO), 67.2 ( $\text{CH}_2$ ), 49.7 ( $\text{CH}_2$ ), 49.1 ( $\text{CH}_2$ ), 22.3 ( $\text{CH}_2$ ), 21.8 ( $\text{CH}_2$ ), 11.7 ( $\text{CH}_3$ ). HRMS calcd for  $\text{C}_{14}\text{H}_{22}\text{NO}_2$  236.1666, found 236.1645.

**(-)-(((S)-2-methylbutoxy)methyl)benzene(18b):** Starting from (-)-(((S)-2-methylbut-3-enyloxy)methyl)benzene (**18a**) with an ee of 92%. Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. (99% yield):

$^1\text{H-NMR}$   $\delta$  7.34 (d,  $J$  = 4.5 Hz, 4H), 7.32-7.23 (m, 1H), 4.53 (s, 2H), 3.36 (m, 1H), 3.28 (m, 1H), 1.72 (m, 1H), 1.51 (m, 1H), 1.18 (m, 1H), 0.94 (m, 6H);  $^{13}\text{C-NMR}$   $\delta$  139.1 (C), 128.5 (CH), 127.7 (CH), 127.6 (CH), 76.0 (CH<sub>2</sub>), 73.2 (CH<sub>2</sub>), 35.3 (CH), 26.5 (CH<sub>2</sub>), 16.9 (CH<sub>3</sub>), 11.6 (CH<sub>3</sub>); HRMS [ $\text{M} + \text{NH}_4^+$ ] calcd for C<sub>12</sub>H<sub>19</sub>O<sub>6</sub> 196.1701, found 196.1695. Enantioselectivity was determined by chiral HPLC analysis, Chiralcel OD-H (99.75% heptane/ 0.25% i-PrOH), 40 °C, retention times (min): 9.7 (major) and 9.9 (minor).

**Racemic ((2-methylbutoxy)methyl)benzene(17c):** was obtained by reduction of racemic ((2-methylbut-3-enyloxy)methyl)benzene following the same procedure as for **17b**. Purification by extraction with 4x 5 ml pentane followed by washing of the organic layer with brine and evaporation of the solvent afforded a yellow oil. (99% yield)

**(+)-1-ethyl-4-isopropylcyclohexene (19b)<sup>11</sup>:** starting from (+)-limonene with an ee of 87%. Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. (72% yield, 90% ee)  $^1\text{H-NMR}$   $\delta$  5.32 (s, 1H), 4.79-1.08 (m, 8H), 1.64 (s, 3H), 0.99-0.72 (m, 6H);  $^{13}\text{C-NMR}$   $\delta$  133.6 (C), 120.7 (CH), 39.7 (CH), 32.0 (CH), 30.5 (CH<sub>2</sub>), 28.6 (CH<sub>2</sub>), 26.2 (CH), 23.1 (CH<sub>3</sub>), 19.7 (CH<sub>3</sub>), 19.4 (CH<sub>3</sub>); The ee was determined using GC with a Chiraldex B-PM column, 50 °C for 5 min followed by heating to 150 °C in 10 min. After 15 min at 150 °C cooling to 50 °C in 15 min.

**(-)-1-ethyl-4-isopropylcyclohexene (20b)<sup>11</sup>:** starting from (-)-limonene with an ee of 99+%. Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. (89% yield, 99+% ee).  $^1\text{H-NMR}$   $\delta$  5.32 (s, 1H), 4.79-1.08 (m, 8H), 1.64 (s, 3H), 0.99-0.72 (m, 6H);  $^{13}\text{C-NMR}$   $\delta$  133.6 (C), 120.7 (CH), 39.7 (CH), 32.0 (CH), 30.5 (CH<sub>2</sub>), 28.6 (CH<sub>2</sub>), 26.2 (CH), 23.1 (CH<sub>3</sub>), 19.7 (CH<sub>3</sub>), 19.4 (CH<sub>3</sub>). The ee was determined using GC with a Chiraldex B-PM column, 50 °C for 5 min followed by heating to 150 °C in 10 min. After 15 min at 150 °C cooling to 50 °C in 15 min.

**10-undecen-1-ol coupled to 2-chlorotrityl chloride polymer resin.** To 0.5 gram of 2-chlorotrityl chloride polymer resin (0.5-0.7 mmol Cl per gram) in 5 ml dry THF was added 119 mg undecanol (0.7 mmol) and 110 mg pyridine (1.4 mmol). The mixture was shaken for 6 hours at 60 °C after which the resin was filtered and washed 3 times with DCM/MeOH/DIEA (17/2/1), 3 times with DCM, 3 times with DMF and 3 times with methanol. After drying in vacuum over KOH, 450 mg of product was obtained.

#### **Cleavage of 10-undecen-1-ol from 2-chlorotrityl polymer resin**

To 150 mg of the resin loaded with 10-undecen-1-ol was added 3 ml CDCl<sub>3</sub> and 0.01 ml TFA. The mixture was shaken for two hours. The resin was filtered and the amount of undecanol was determined by  $^1\text{H NMR}$  to be 0.26 mmol per gram, by applying TMS as an internal standard.

**Reduction of 10-undecen-1-ol coupled to 2-chlorotrityl chloride polymer resin.** To 500 mg of resin was added 3.5 ml EtOH, 0.5 ml hydrazine hydrate, and 10 mg 5-ethyl-riboflavin catalyst **1a**. The reaction vessel was shaken for 24 hours under an O<sub>2</sub> atmosphere (balloon). Afterwards, the resin was filtered and washed 3 times with dichloromethane and three times with MeOH.

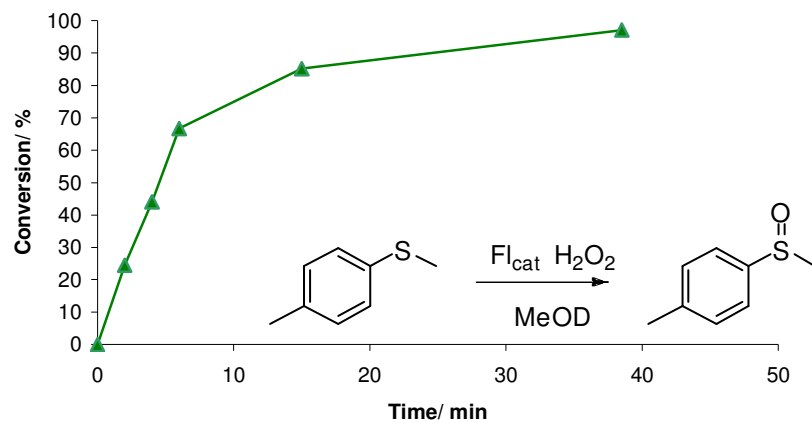
#### **Cleavage of 10-undecanol from 2-chlorotrityl chloride polymer resin**

To 150 mg of resin was added 3 ml CDCl<sub>3</sub> and 0.01 ml TFA. The mixture was shaken for two hours. The resin was filtered and the yield of the product was determined by  $^1\text{H NMR}$  by addition of 10  $\mu\text{L}$  TMS (72.5  $\mu\text{mol}$ ) as internal standard. 90% yield, >95% (GC-MS), no remaining undecanol was observed.

#### **Oxidation of 4-methylphenylmethyl sulfoxide (2a) with flavin catalyst 1a**

In a NMR tube with 600  $\mu\text{L}$  methanol-*d*<sub>4</sub> was added 1.58 mg **1a** (4  $\mu\text{mol}$ ) and 30  $\mu\text{L}$  methyl-*p*-tolyl sulfide (2.2 mmol). 40  $\mu\text{L}$  H<sub>2</sub>O<sub>2</sub> (30% in H<sub>2</sub>O, 3.5 mmol) was added and the reaction was followed in time using  $^1\text{H-NMR}$ <sup>12</sup> (See Figure 1)

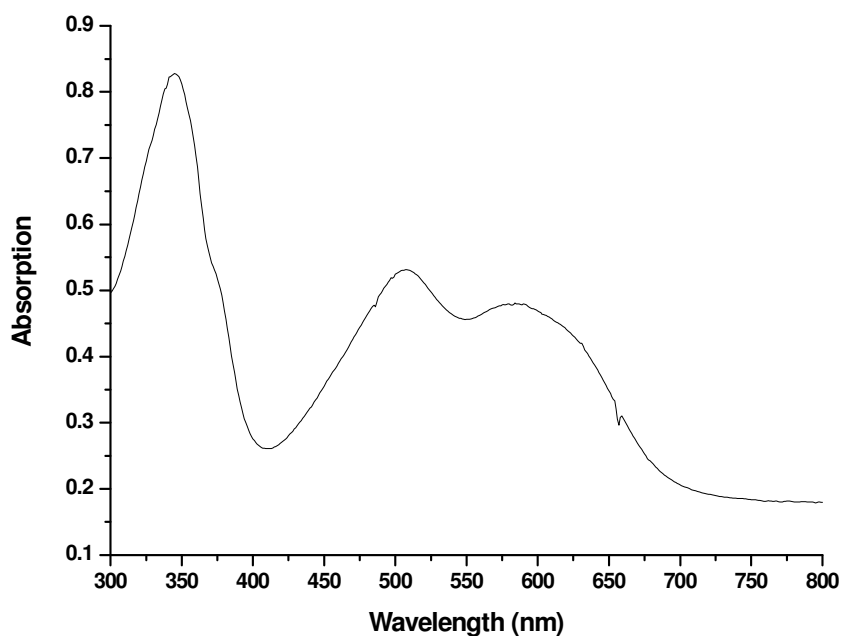
**Figure 1:** Conversion of 4-methylphenyl methyl sulfide into 4-methylphenyl methyl sulfoxide



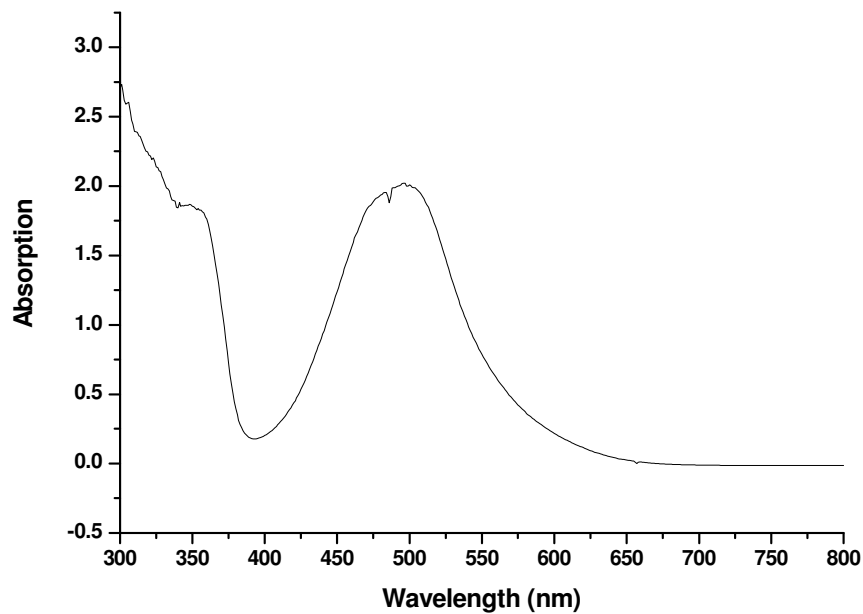
### UV spectra of **1a** and **1b**:

The nomenclature of the spectra is derived from the work of Bruice et al.<sup>13</sup> Catalyst **1a** and **1b** show the same UV-spectra, measured with 1.9 mg catalyst/10 ml in H<sub>2</sub>O (0.47 mM). the catalyst can be found in a number of different distinct states:

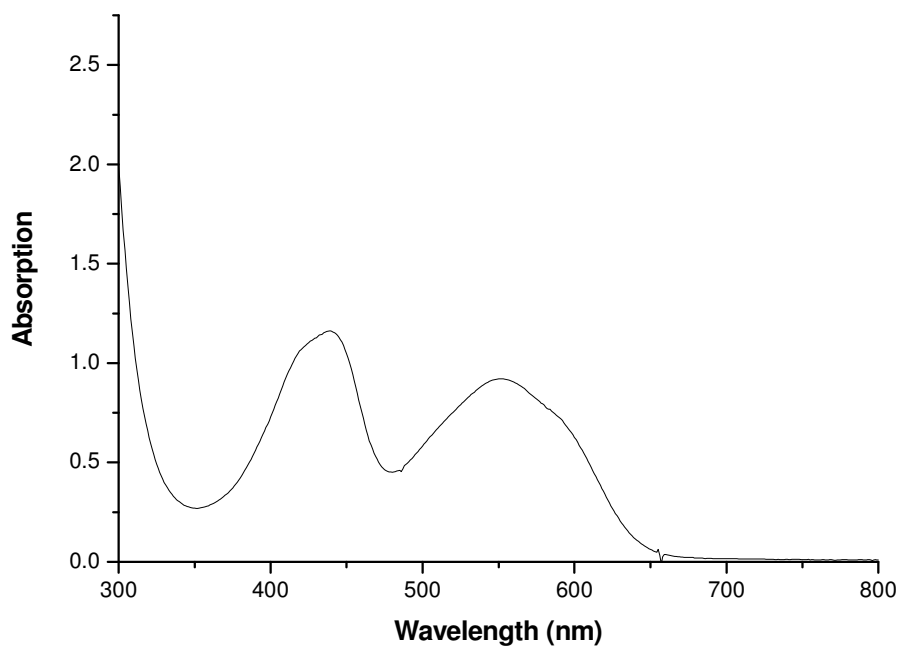
- 1) "Blue colored radical" (semiquinone species) (0.47 mM catalyst in pure H<sub>2</sub>O)



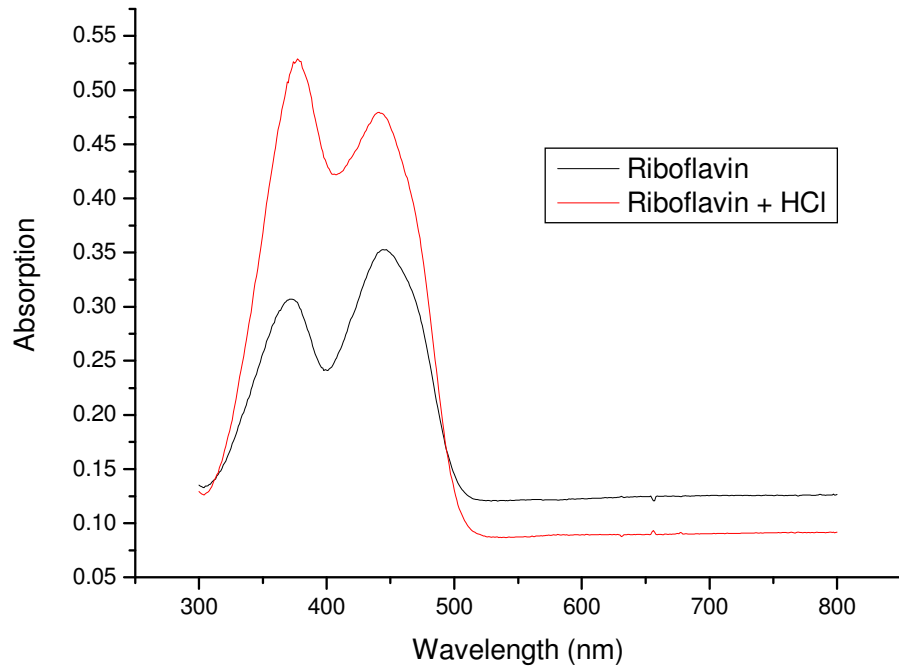
- 2) "Pink protonated radical" (0.47 mM catalyst in H<sub>2</sub>O + 16.6  $\mu$ L 6N HCl)



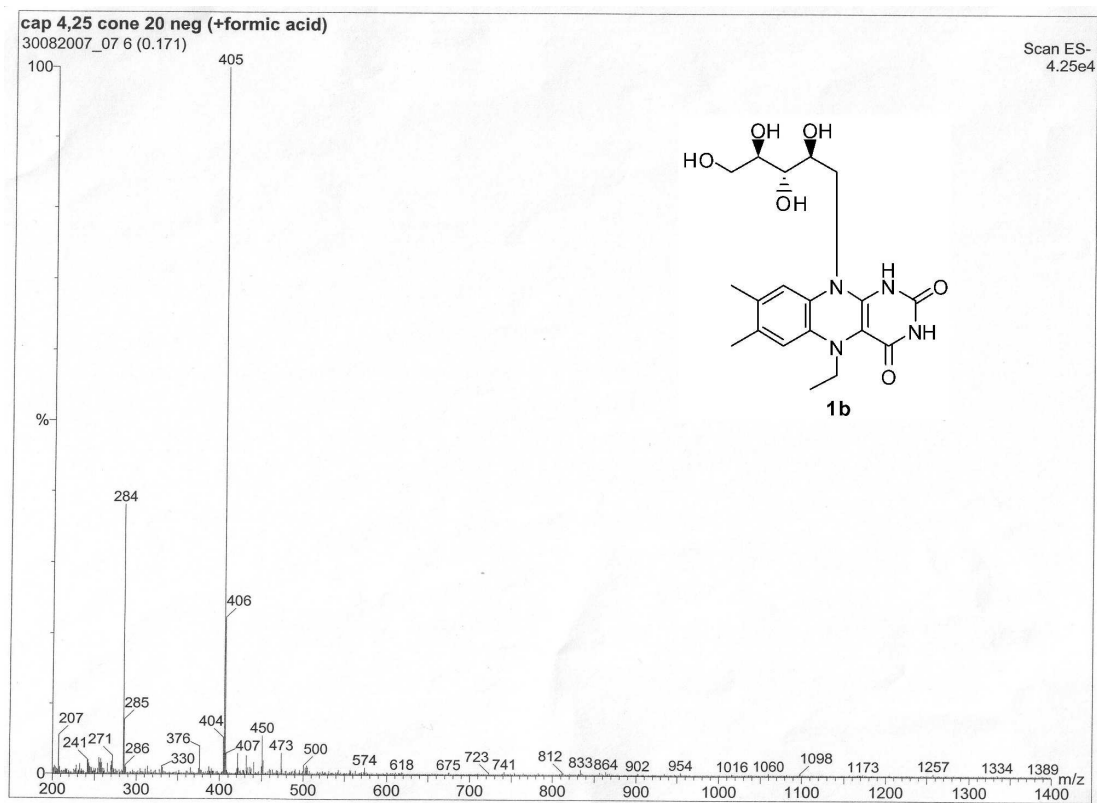
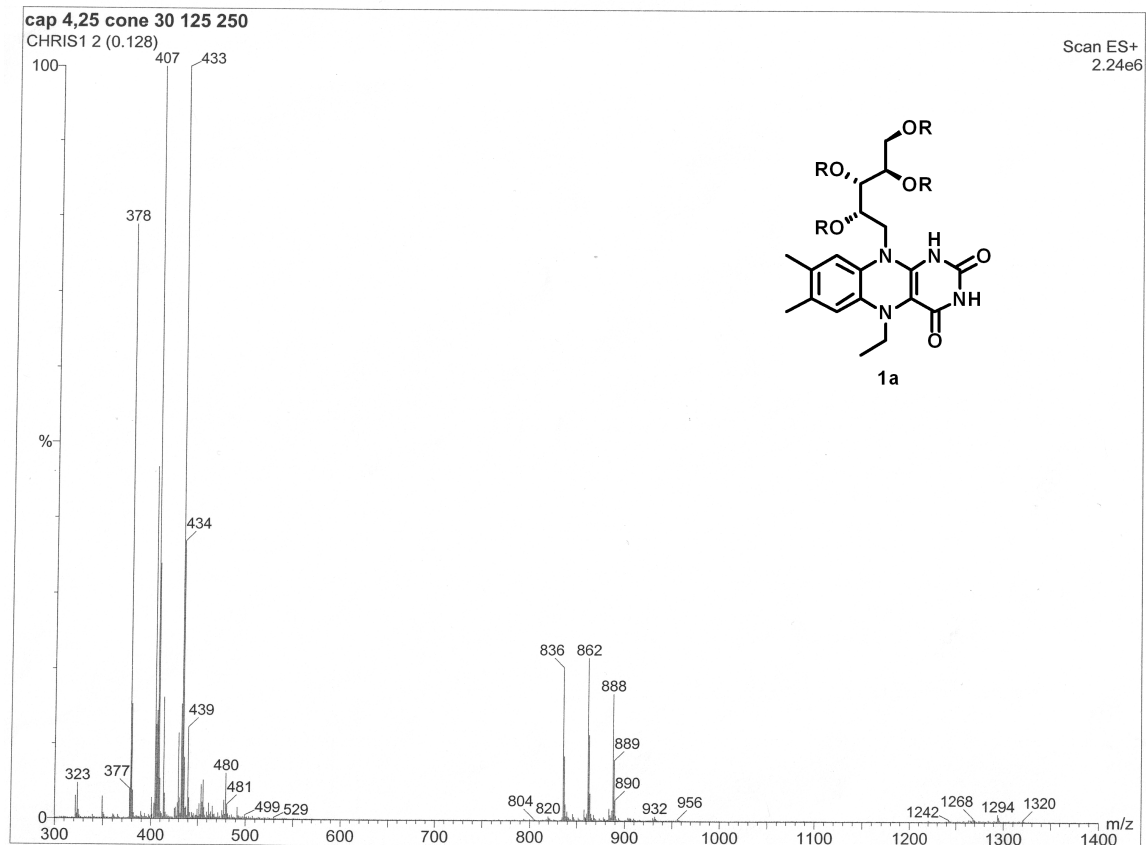
3) “Red Flavinium cation” (0.47 mM catalyst in H<sub>2</sub>O + 16.6  $\mu$ L 6N HCl + 50  $\mu$ L 30% H<sub>2</sub>O<sub>2</sub>)

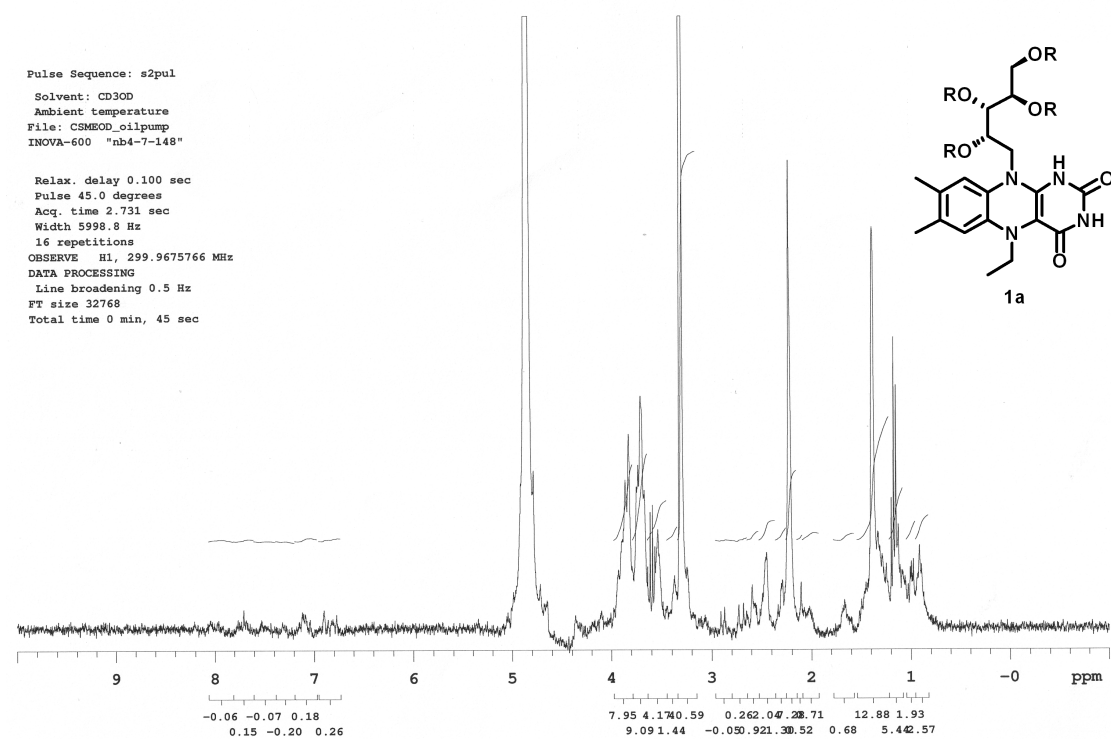
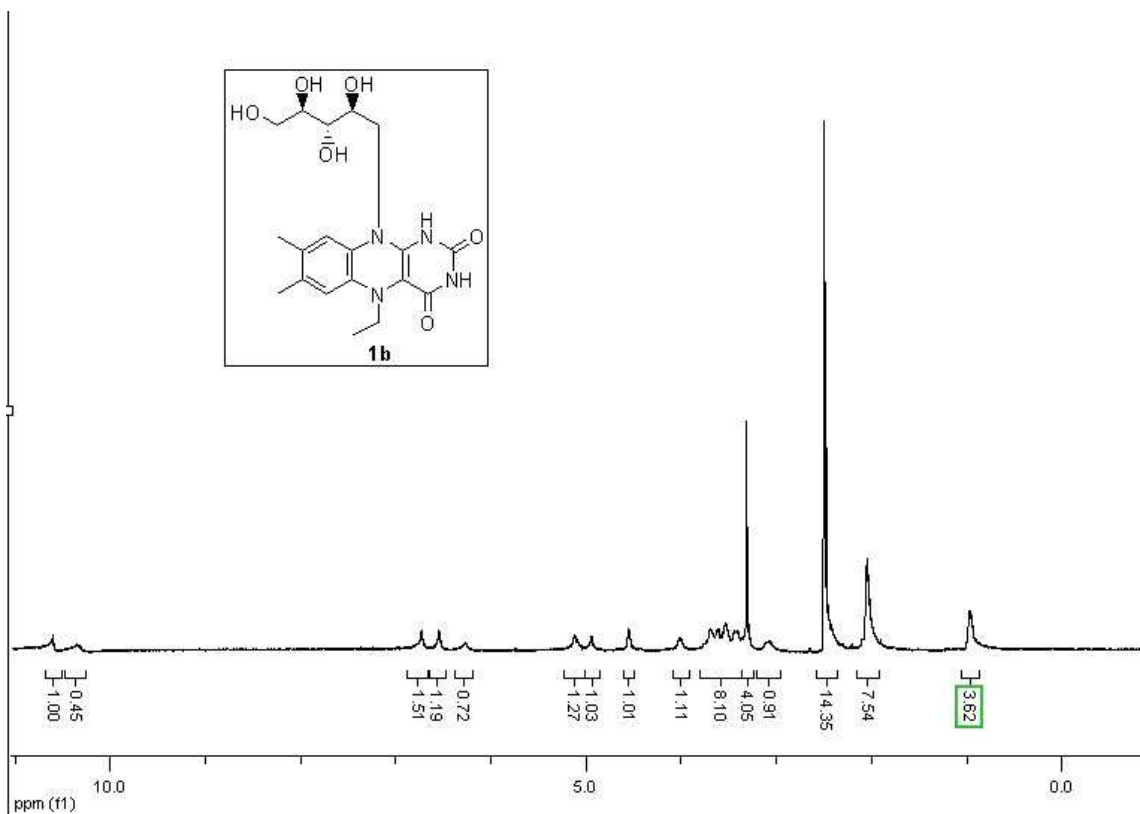


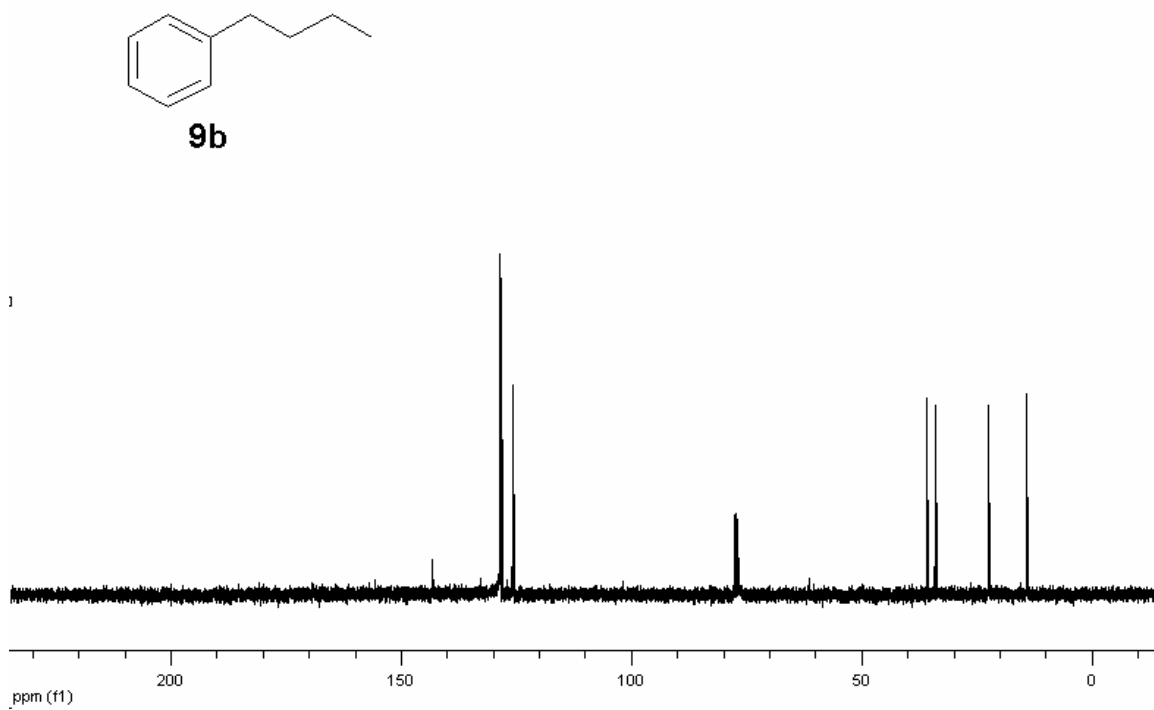
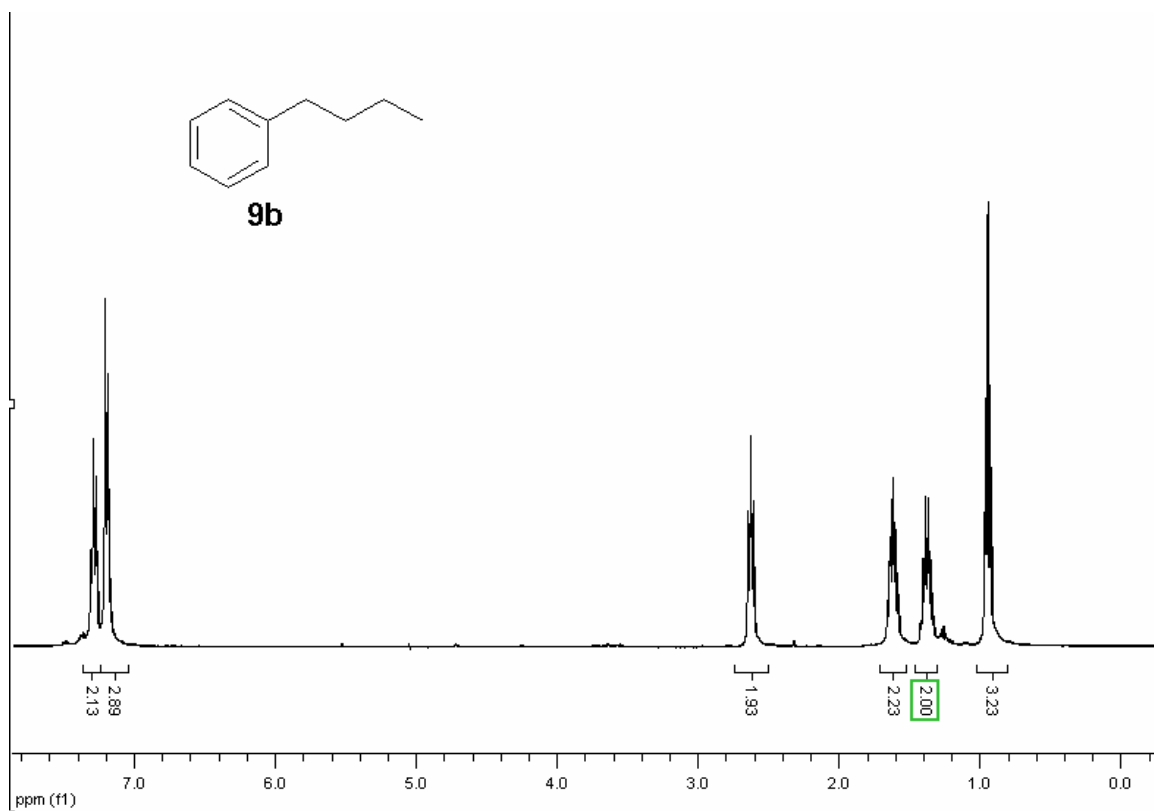
4) Riboflavin (starting material)

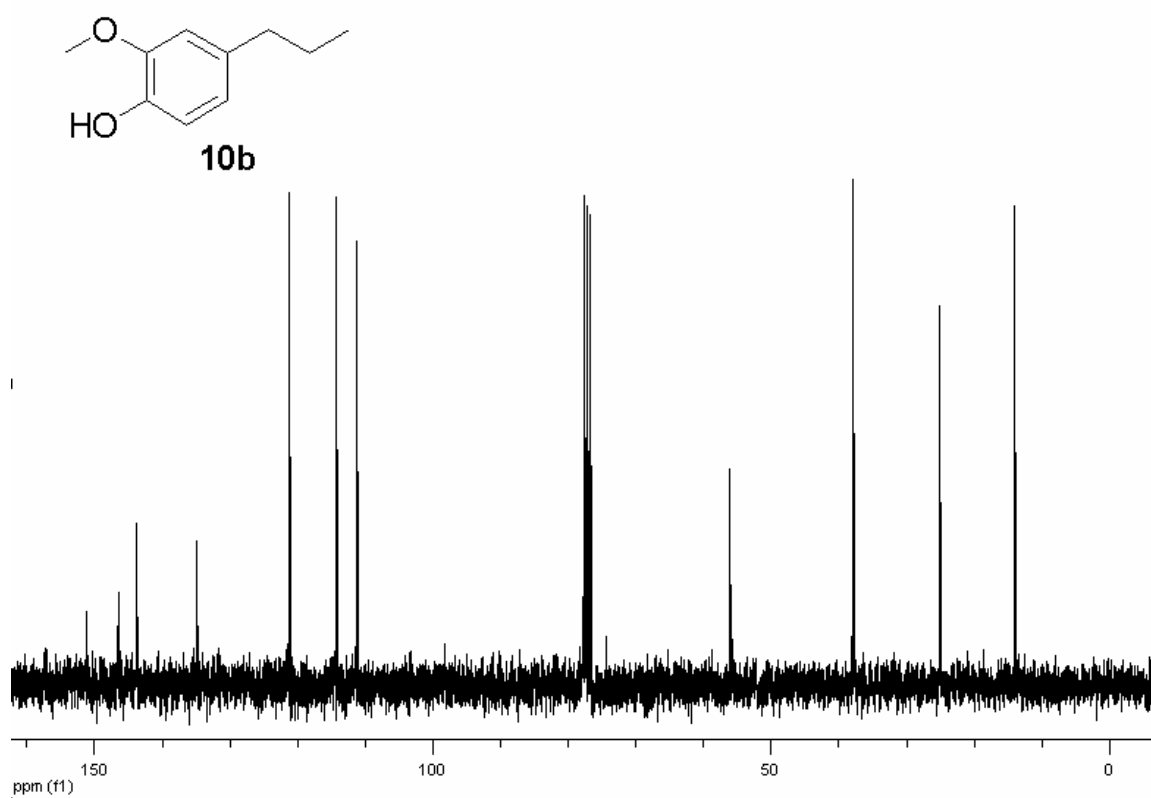
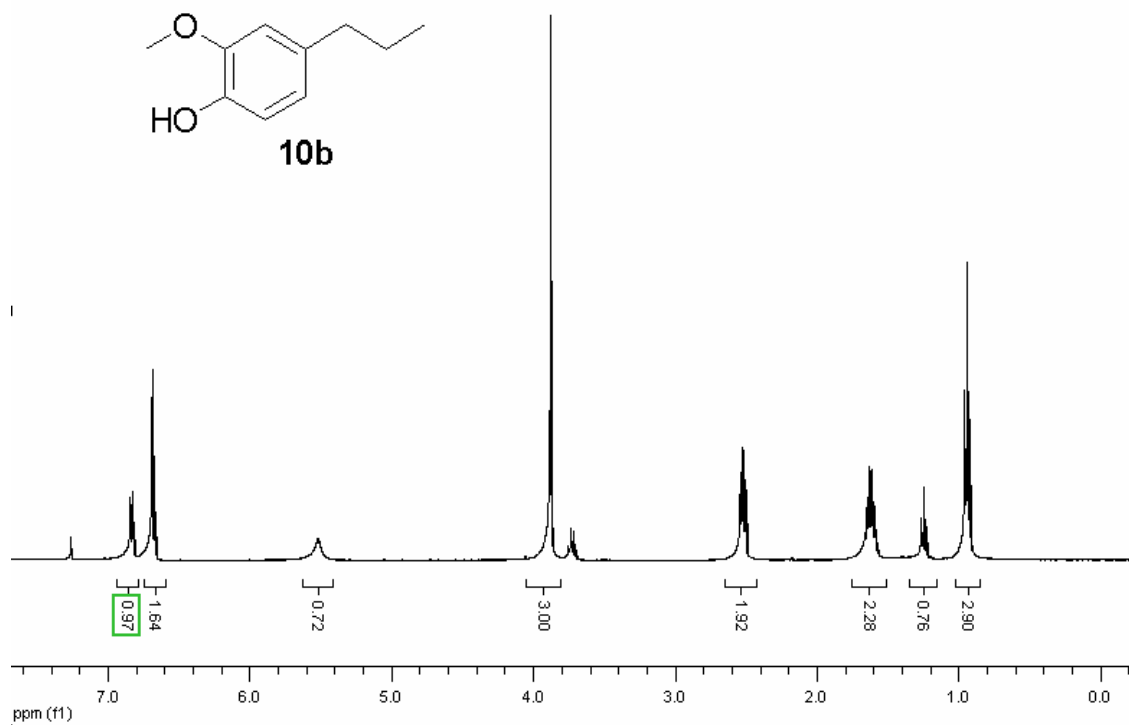




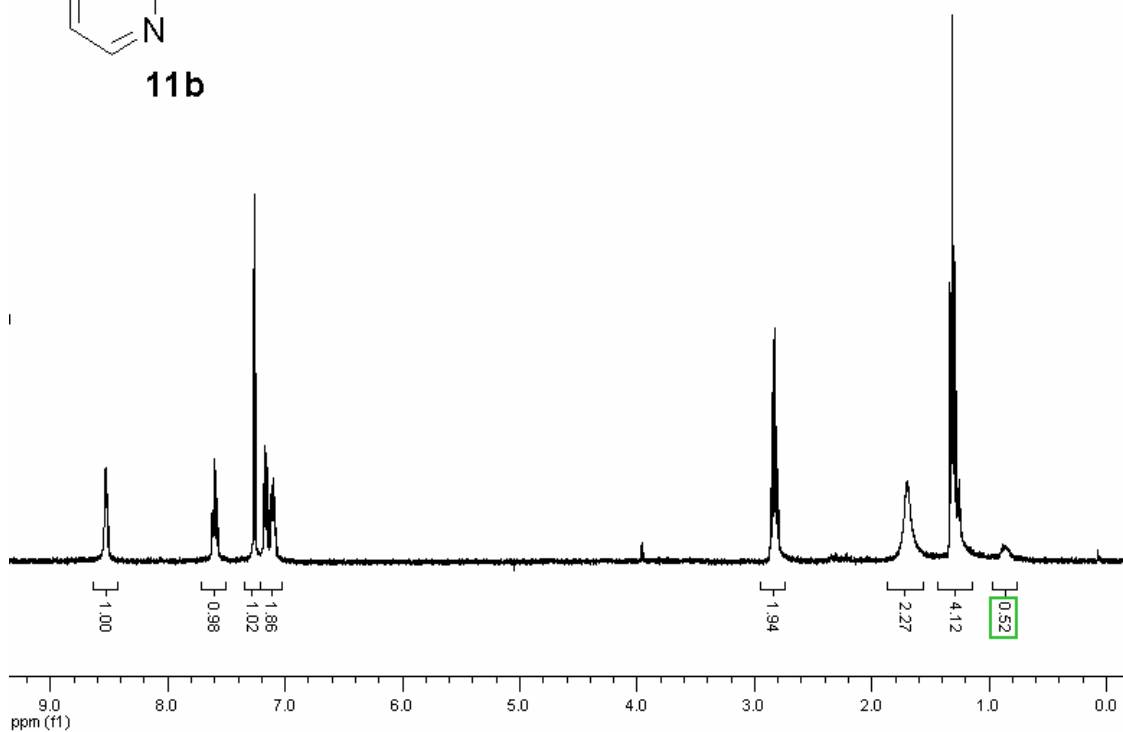
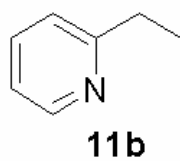
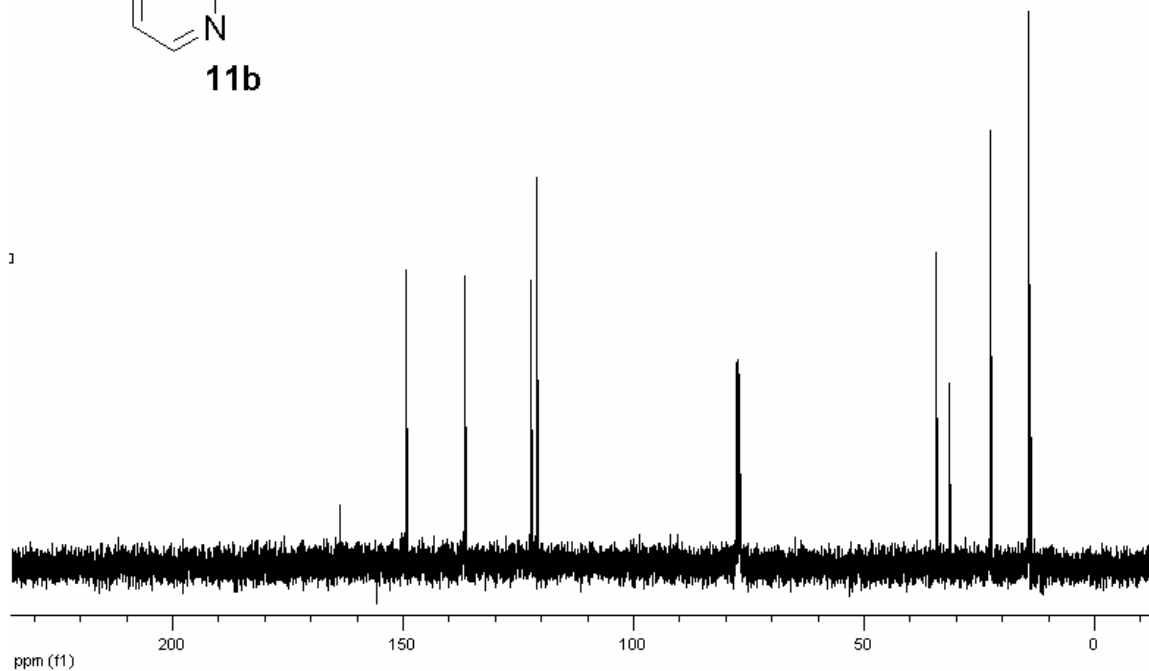
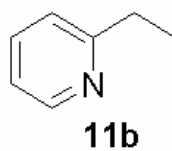


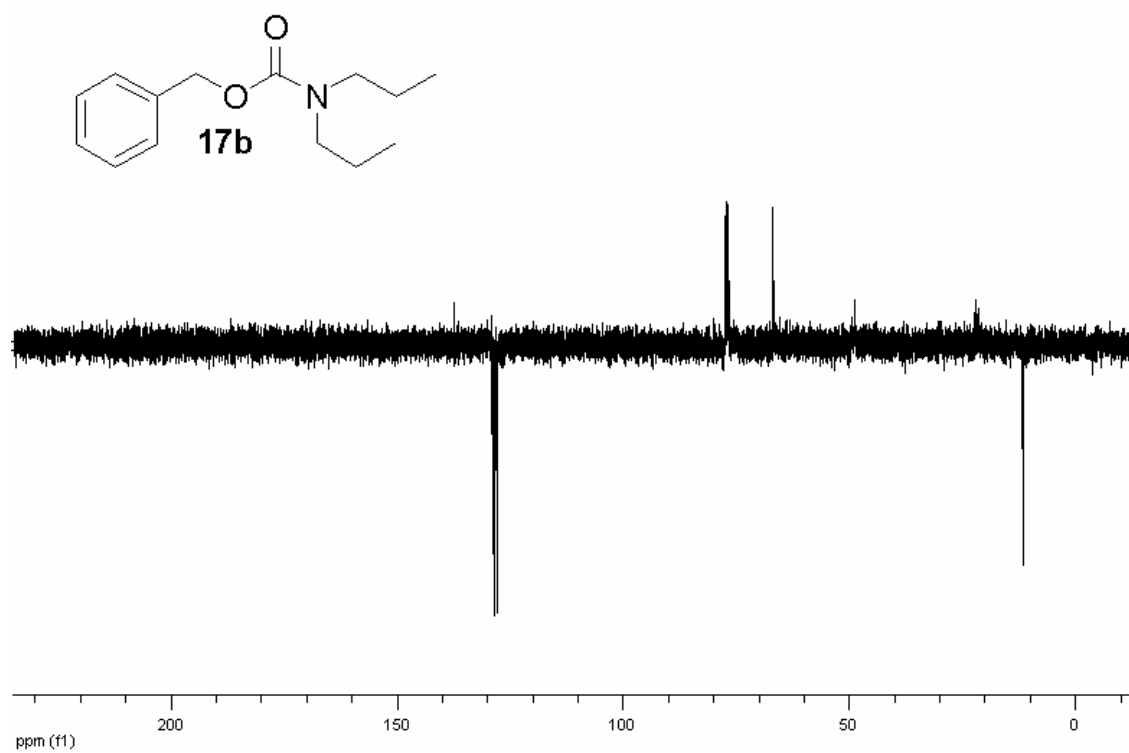
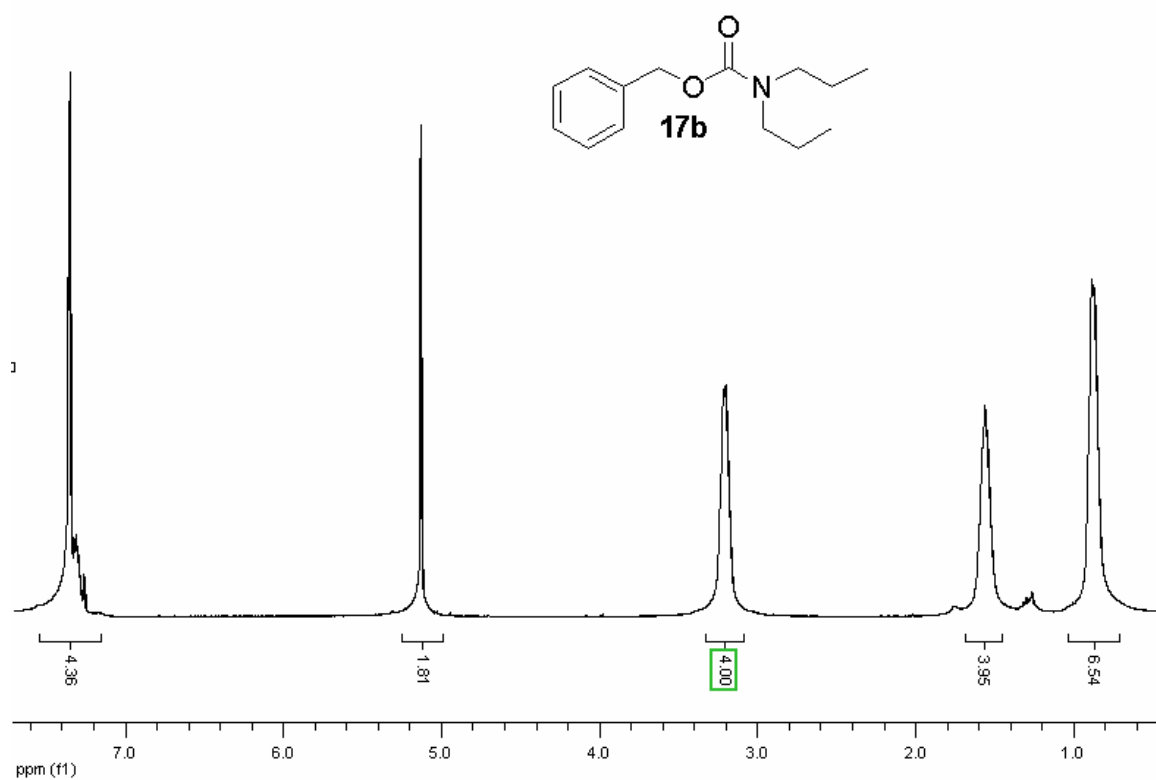


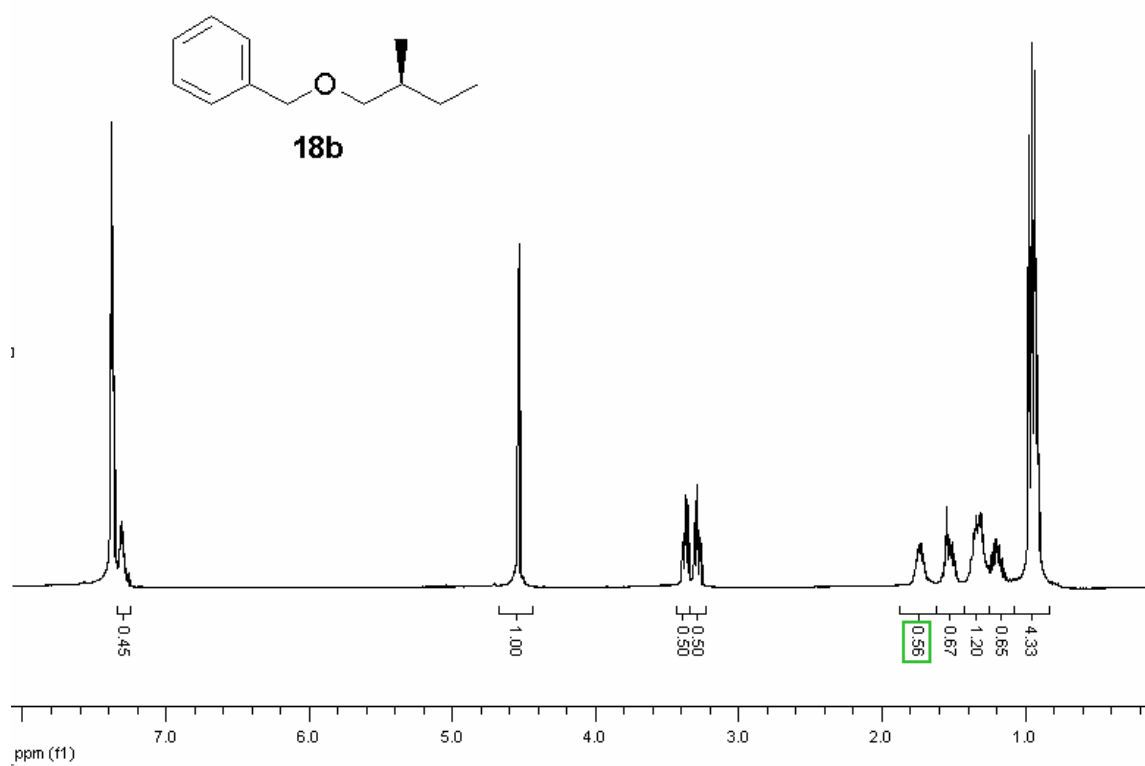
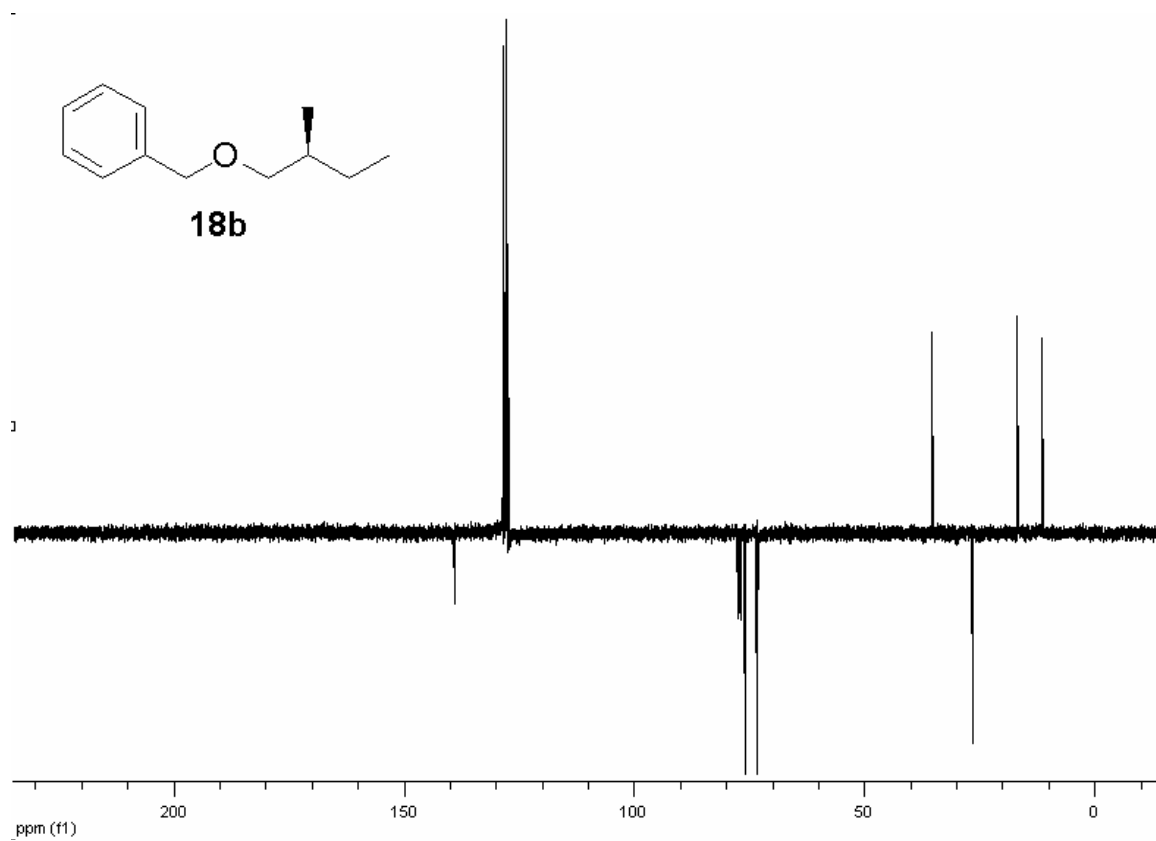




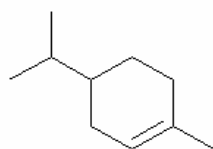
Due to the volatile nature of this compound, not all the pentane could be removed



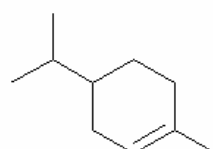
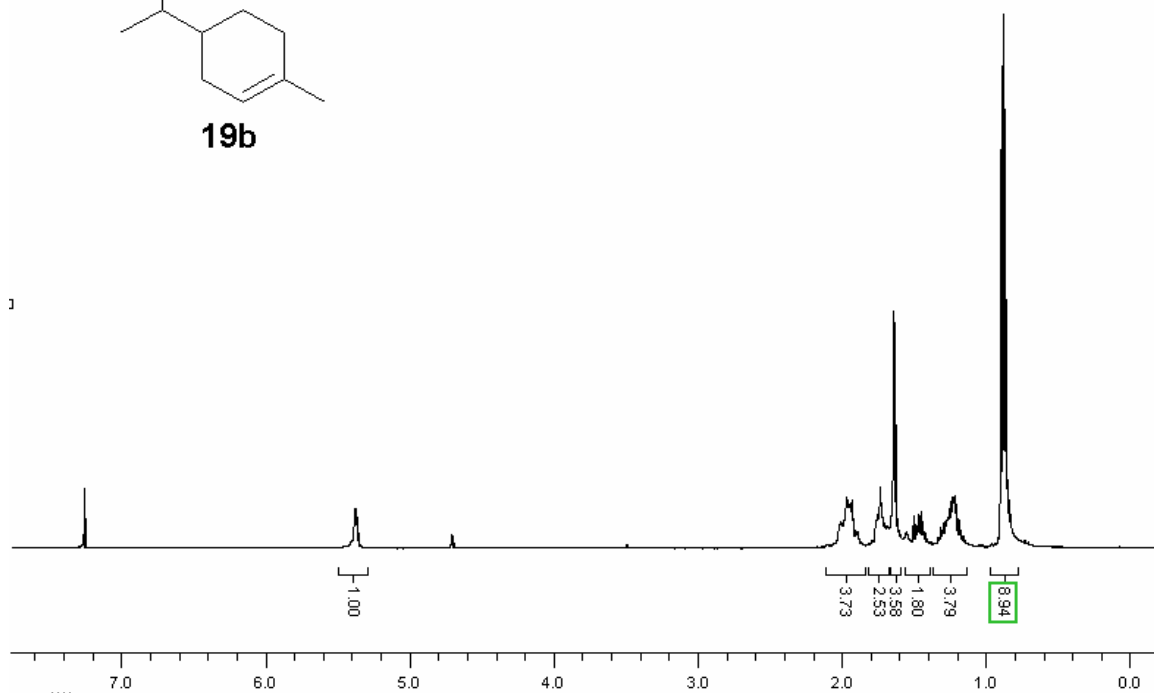




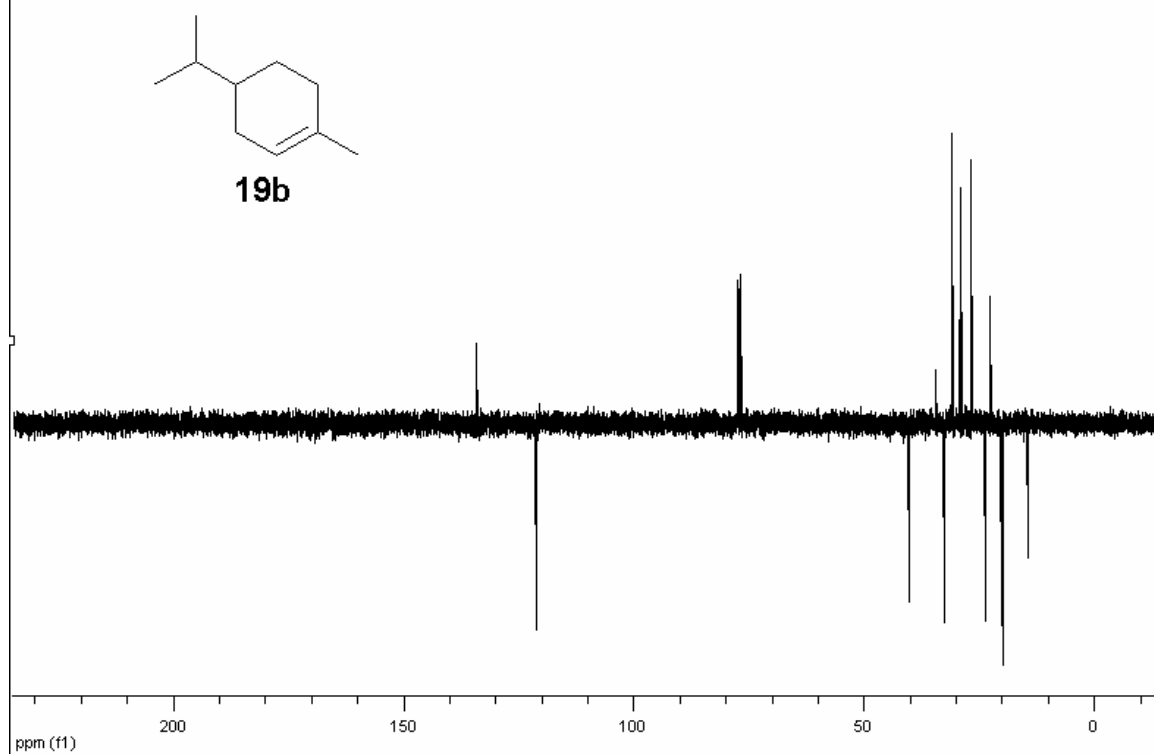
Due to the volatile nature of this compound, not all pentane could be removed



**19b**



**19b**





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